

**EXHIBIT B**  
**PENDING CLAIMS**  
U.S. PATENT APPLICATION SERIAL NO. 09/625,137  
(ATTORNEY DOCKET 8449-123)  
(as amended under 37 C.F.R. §1.111)

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1. A method for identifying a compound that modulates a heat shock protein (HSP)-alpha (2) macroglobulin ( $\alpha$ 2M) receptor-mediated process, comprising:
  - (a) contacting a test compound with: (i) an isolated alpha (2) macroglobulin receptor, or a ligand-binding fragment thereof; and (ii) a purified heat shock protein, or a binding fragment thereof, or a purified HSP-peptide complex; and
  - (b) measuring the level of alpha (2) macroglobulin receptor activity or expression, such that if the level of activity or expression measured in (b) differs from the level of alpha (2) macroglobulin receptor activity in the absence of the test compound, then a compound that modulates an HSP- $\alpha$ 2M receptor-mediated process is identified.
2. The method of claim 1, in which the compound identified is an antagonist which interferes with an HSP- $\alpha$ 2M receptor-mediated process.
3. The method of claim 1, in which the test compound is an antibody specific for the alpha (2) macroglobulin receptor.
4. The method of claim 1, in which the test compound is an antibody is specific for alpha (2) macroglobulin.
5. The method of claim 1, in which the test compound is an antibody is specific for a heat shock protein.
6. The method of claim 1, in which the test compound is a small molecule.
7. The method of claim 1, in which the test compound is a peptide.
8. The method of claim 7, in which the peptide comprises at least 5 consecutive amino acids of the alpha (2) macroglobulin receptor (SEQ ID NO.: 7).

9. The method of claim 7, in which the peptide comprises at least 5 consecutive amino acids of alpha (2) macroglobulin (SEQ ID NO.: 4).

10. The method of claim 7, in which the peptide comprises at least 5 consecutive amino acids of a heat shock protein sequence.

11. The method of claim 1, in which the compound is an agonist which enhances an HSP- $\alpha$ 2M receptor-mediated process.

12. The method of claim 1 in which the HSP- $\alpha$ 2M receptor-mediated process affects an autoimmune disorder, a disease or disorder involving disruption of antigen presentation or endocytosis, a disease or disorder involving cytokine clearance or inflammation, a proliferative disorder, a viral disorder or other infectious disease, hypercholesterolemia, Alzheimer's disease, diabetes, or osteoporosis.

13. A method for identifying a compound that modulates an HSP- $\alpha$ 2M receptor-mediated process, comprising:

- (a) contacting a test compound with an alpha (2) macroglobulin receptor- or ligand binding fragment- expressing cell and a purified heat shock protein, or fragment thereof, or a purified HSP-peptide complex; and
- (b) measuring the level of alpha (2) macroglobulin receptor binding activity in the cell,

such that if the level of alpha (2) macroglobulin receptor binding activity measured in (b) differs from the level of alpha (2) macroglobulin receptor activity in the absence of the test compound, then a compound that modulates an HSP- $\alpha$ 2M receptor-mediated process is identified.

14. The method of claim 1 or 13 wherein the alpha (2) macroglobulin receptor activity measured is the ability to bind to a heat shock protein.

17. The method of claim 1 or 13 wherein the alpha (2) macroglobulin receptor activity measured is the ability to bind to a heat shock protein, wherein measuring the level of alpha (2) macroglobulin receptor activity of step (b) comprises measuring the amount of heat

shock protein, or binding fragment thereof, bound to the alpha (2) macroglobulin receptor, or ligand-binding fragment thereof,

such that if the amount of bound heat shock protein measured in (b) differs from the amount of bound heat shock protein measured in the absence of the test compound, then a compound that modulates the binding of an HSP to the  $\alpha$ 2M receptor is identified.

18. The method of claim 1 or 14, in which the alpha (2) macroglobulin receptor contacted in step (a) is on a cell surface.

19. The method of claim 1 or 14, wherein the alpha (2) macroglobulin receptor is immobilized to a solid surface.

20. The method of claim 19 wherein the solid surface is a microtiter dish.

21. The method of claim 14 wherein the amount of bound heat shock protein is measured by contacting the cell with a heat shock protein-specific antibody.

22. The method of claim 14 wherein the heat shock protein is labeled and the amount of bound heat shock protein is measured by detecting the label.

23. The method of claim 22 wherein the heat shock protein is labeled with a fluorescent label.

64. The method of claim 1 or 13, wherein the alpha (2) macroglobulin receptor is purified.

65. The method of claim 1 or 13, wherein the expression measured is alpha (2) macroglobulin receptor gene expression.

66. The method of claim 1 or 13, wherein the expression measured is alpha (2) macroglobulin receptor gene product expression.

67. The method of claim 14, wherein the {derivative, analog, fragment,} or domain of the alpha (2) macroglobulin receptor is purified.

68. A method for identifying a compound that modulates an HSP- $\alpha$ 2M receptor-mediated process, comprising:

- (a) contacting a test compound with an alpha (2) macroglobulin receptor-expressing cell and a purified heat shock protein, or {fragment thereof,} or a purified HSP-peptide complex; and
- (b) measuring the level of alpha (2) macroglobulin receptor activity by a signal transduction activity assay, heat shock protein uptake assay, chemotaxis assay, or calcium ion concentration assays,

such that if the level of alpha (2) macroglobulin receptor activity measured in (b) differs from the level of alpha (2) macroglobulin receptor activity in the absence of the test compound, then a compound that modulates an HSP- $\alpha$ 2M receptor-mediated process is identified.

69. A method for screening a plurality of molecules for one or more molecules having the ability to modulate, directly or indirectly, the antigen presentation activity of alpha (2) macroglobulin receptor-expressing cells, comprising:

- (a) contacting said plurality of molecules with the alpha (2) macroglobulin receptor-expressing cells and a purified complex of a heat shock protein and the antigenic peptide;
- (b) measuring antigen presentation by said alpha (2) macroglobulin receptor-expressing cells in the presence of said plurality of molecules; and
- (c) comparing antigen presentation activity by said alpha (2) macroglobulin receptor-expressing cells in the presence of said plurality of molecules with antigen presentation activity by said alpha (2) macroglobulin receptor-expressing cells in the absence of said plurality of molecules

wherein a lower or higher degree of antigen presentation indicates that one or more molecule(s) modulates the antigen presentation activity by said alpha (2) macroglobulin receptor-expressing cells.

70. A method for screening an antibody specific to a heat shock protein or an alpha (2) macroglobulin receptor for the ability to modulate, directly or indirectly, the antigen presentation activity of alpha (2) macroglobulin receptor-expressing cells, comprising:

- (a) contacting the antibody with the alpha (2) macroglobulin receptor-expressing cells and a purified complex of a heat shock protein and the antigenic peptide;
- (b) measuring antigen presentation by the alpha (2) macroglobulin receptor-expressing cells in the presence of the antibody; and
- (c) comparing antigen presentation activity by said alpha (2) macroglobulin receptor-expressing cells in the presence of the antibody with antigen presentation activity by the alpha (2) macroglobulin receptor-expressing cells in the absence of the antibody,

wherein a lower or higher degree of antigen presentation indicates that the antibody modulates the antigen presentation activity by said alpha (2) macroglobulin receptor-expressing cells.

71. A method for screening a molecule for the ability to modulate, directly or indirectly, the antigen presentation activity of alpha (2) macroglobulin receptor-expressing cells, comprising:

- (a) contacting the molecule with purified alpha (2) macroglobulin receptor-expressing cells and a purified complex of a heat shock protein and an antigenic peptide;
- (b) measuring antigen presentation by the alpha (2) macroglobulin receptor-expressing cells in the presence of the molecule; and
- (c) comparing antigen presentation activity by the alpha (2) macroglobulin receptor-expressing cells in the presence of the molecule with antigen presentation activity by the alpha (2) macroglobulin receptor-expressing cells in the absence of the molecule,

wherein a lower or higher degree of antigen presentation indicates that the molecule modulates the antigen presentation activity by said alpha (2) macroglobulin receptor-expressing cells.

72. A method for screening a plurality of molecules for one or more molecules having the ability to modulate, directly or indirectly, the ability of an alpha (2) macroglobulin receptor-expressing cell to stimulate the activation of cytotoxic T cells *in vitro* comprising:

- (a) contacting said plurality of molecules with: (i) cells expressing alpha (2) macroglobulin receptor; (ii) a purified complex of a heat shock protein and a peptide; and (iii) cytotoxic T cells, under conditions conducive to the activation of cytotoxic T cells;
- (b) comparing the activation *in vitro* of said T cells with the activation *in vitro* of T cells in the absence of said plurality of molecules,

wherein a lower or higher degree of T cell activation indicates that one or more molecules in said plurality of molecules modulates the ability of the alpha (2) macroglobulin -expressing cells to stimulate the activation of cytotoxic T cells against the peptide.

73. A method for screening an antibody specific to a heat shock protein or an alpha (2) macroglobulin receptor for the ability to modulate, directly or indirectly, the ability of an alpha (2) macroglobulin receptor-expressing cell to stimulate the activation of cytotoxic T cells *in vitro* comprising:

- (a) contacting the antibody with: (i) cells expressing alpha (2) macroglobulin receptor; (ii) a purified complex of a heat shock protein and a peptide; and (iii) cytotoxic T cells, under conditions conducive to the activation of cytotoxic T cells;
- (b) comparing the activation *in vitro* of said T cells with the activation *in vitro* of T cells in the absence of said plurality of molecules,

wherein a lower or higher degree of T cell activation indicates that the antibody modulates the ability of the alpha (2) macroglobulin -expressing cells to stimulate the activation of cytotoxic T cells against the peptide.

74. A method for screening a molecule for the ability to modulate, directly or indirectly, the ability of an alpha (2) macroglobulin receptor-expressing cell to stimulate the activation of cytotoxic T cells *in vitro* comprising:

- (a) contacting said molecule with: (i) purified cells expressing alpha (2) macroglobulin receptor; (ii) a purified complex of a heat shock protein and a

peptide; and (iii) cytotoxic T cells, under conditions conducive to the activation of cytotoxic T cells;

- (b) comparing the activation *in vitro* of said T cells with the activation *in vitro* of T cells in the absence of said plurality of molecules,

wherein a lower or higher degree of activation indicates that one or more molecules in said plurality of molecules modulates the ability of the alpha (2) macroglobulin -expressing cells to stimulate the activation of cytotoxic T cells against the peptide.

75. The method of any one of claims 70, 71, or 72, wherein the activity is measured by a cytokine release assay.

76. The method of any one of claims 13, 69, 70, 71, 72, 73, or 74, wherein the alpha (2) macroglobulin receptor is recombinantly expressed in the cell.